Study of serum ferritin levels as an inflammatory marker and its relationship with Hba1c in type 2 diabetes mellitus

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Abstract

Type 2 diabetes mellitus is the leading metabolic disorder globally as well as in India, affecting more than 135 million people all over the world.[1] Studies have shown a strong association between elevated serum levels of ferritin and type 2 DM.[4] Serum ferritin could be an independent determinant of poor metabolic control in the diabetic patient.[2] Serum ferritin as an inflammatory marker in type 2 diabetes mellitus is an underutilized but can be a reliable tool to evaluate the metabolic disorder.[4] We assessed 180 subjects (120 cases and 60 controls) in the current study. The case group was divided in to 2 groups based on the HbA1c levels as Group B: HbA1C < 6g/dl (60 cases) and Group C: HbA1C > 6g/dl (60 cases). The work embodied in the study includes subjects diagnosed of type 2 diabetes mellitus above 40 years of age, attending diabetic OPD in ESIC PGIMSR, of both gender. Group A (control) includes healthy adults above 30 years of age both the sexes. Serum levels Fasting sugar and Ferritin were estimated along with Glycated hemoglobin levels. Mean serum ferritin levels in Group A, Group B and Group C were 112.08 ± 90.1ng/dl, 334.4 ± 39.1ng/mL and 368.9 ± 46.7 ng/ respectively. Serum ferritin levels in Group B and C were significantly higher than Group A (p <0.001. The study concludes that inflammatory biomarker - ferritin is strongly and independently associated with cardiovascular complications in diabetes.

Keywords: Type 2 diabetes, Serum ferritin, Glycated hemoglobin, Inflammatory marker.

Introduction

Type 2 diabetes mellitus is the leading metabolic disorder globally as well as in India affecting more than 135 million people all over the world.[1] Studies have shown a strong association between elevated serum levels of ferritin and type 2 DM. Serum ferritin could be an independent determinant of poor metabolic control in the diabetic patient.[2] There is enough evidence that shows Increased load of body iron stores causes oxidative stress which further leads to damage of beta cells of pancreas resulting in insulin deficiency.[3]

Frequent blood donation lead to decrease iron stores, which in turn reduces postprandial hyperinsulinemia and improves insulin sensitivity.[4] Serum ferritin as an inflammatory marker in type 2 diabetes mellitus is an underutilized but can be a reliable tool to evaluate the metabolic disorder.[4] There is a gap in information available regarding the poor control of blood glucose levels in diabetics with increased iron stores. Studies pertaining to this in Indian population are very minimal and finding out such correlation can be of high significance with the background of increased prevalence of anemia in the population.[4]

This study aims at estimating the levels of serum ferritin in patients of diabetes in order to establish its significance in the management and to prevent further complications.

Materials and Methods

From the patients who attended the OPD with known diabetes in ESICMS PGIMSR, Bangaluru, a total number of 180 subjects were included. This includes 60 controls Group A and 120 diabetic patients who were divided into 2 sub-groups - Group B: HbA1C < 6 mg/dl and Group C: HbA1C > 6mg/dl. Cases of type 2 diabetes of both gender in the age group >40years attending diabetic OPD in ESIC PGIMSR, Rajajinagar, Bangalore, were included in the study. Patients with anaemia, thalassemia, Hemochromatosis, patients on drugs affecting serum ferritin levels, drug induced diabetes, pancreatic diseases (chronic pancreatitis), cystic fibrosis, endocrinopathies like cushing syndrome, thyrotoxicosis, acromegaly, gestational diabetes, patients with any other chronic infective & inflammatory conditions that may affect serum ferritin levels, were excluded from the study. The control group A includes healthy adult subjects in the age group > 30 years of both the sexes. A volume of 5ml venous blood sample was obtained after 12 hours overnight fasting and processed for the estimation of fasting blood glucose estimation, serum ferritin levels and HbA1C levels.

Serum concentration of glucose was estimated by using analytical kits from Erba Diagnostics Mannheim GmbH in semi-autoanaylzer (CHEM-5 Plus V2, Erba Mannheim).Serum concentrations of ferritin, insulin were estimated by Chemiluminiscence immunoassay (CLIA) kits from Acculite Monobind in Lumax CLIA strip reader. Glycated hemoglobin was estimated by Nephelometry kits from Agappe in MISPA-i card reader.
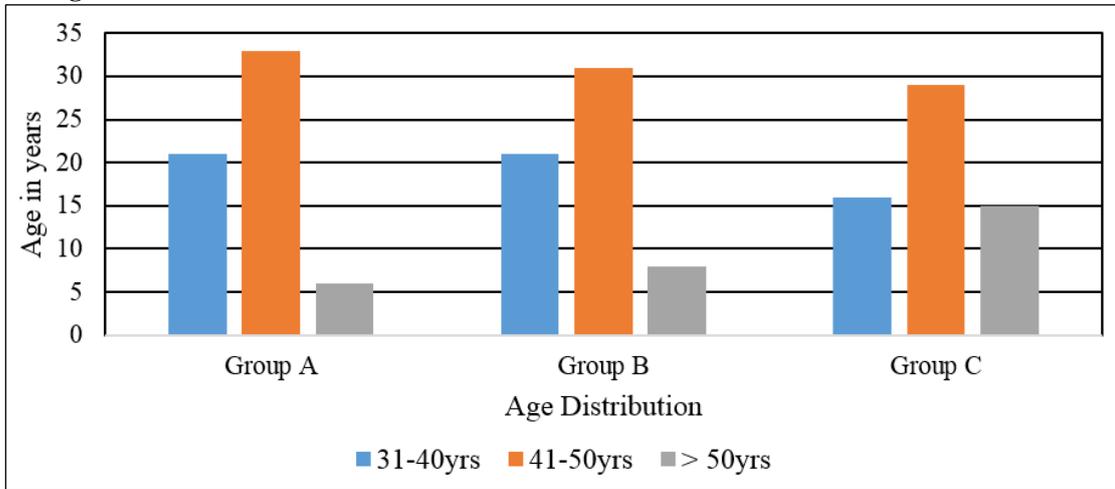
Statistical Analysis

R software has been used for the statistical analysis. The correlations between HbA1C and serum ferritin levels have represented using "Scatter Plots" and the corresponding correlation coefficients (r) have been found out.
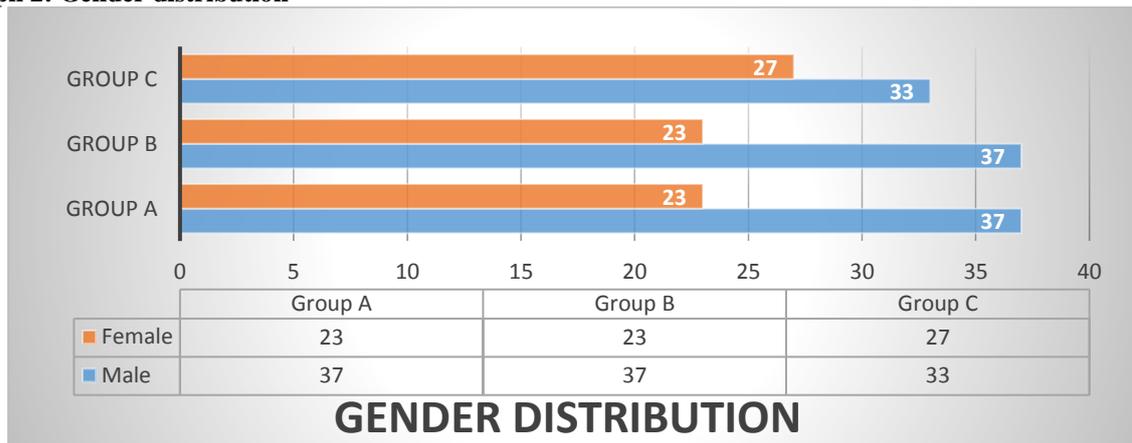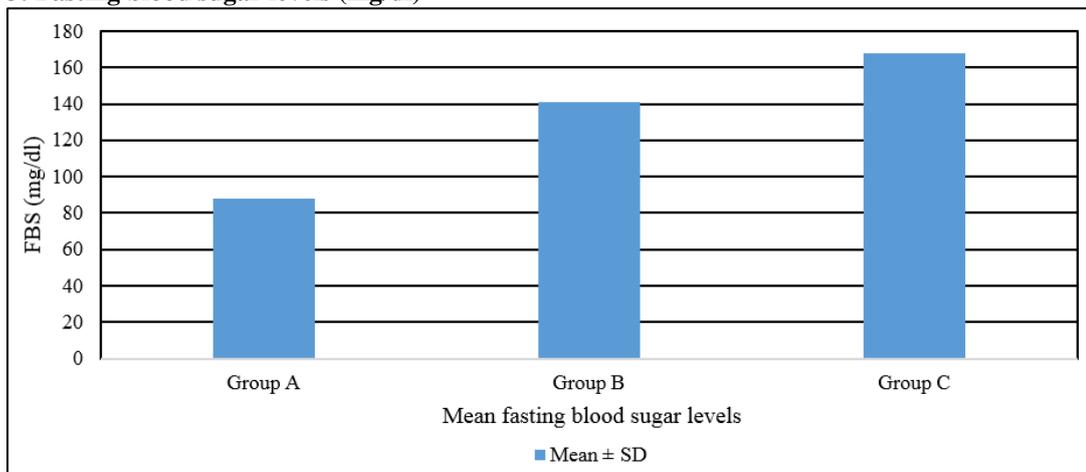
Results

Graph 1: Age distribution

P < 0.0908

Graph 2: Gender distribution

	Group A	Group B	Group C
Female	23	23	27
Male	37	37	33

GENDER DISTRIBUTION

Graph 3: Fasting blood sugar levels (mg/dl)

FBS levels are positively correlated with HbA1c levels and statistically significant (P< 0.001)

Table 1: HbA1C Levels

HbA1C Levels	Group A	Group B	Group C
Mean ± S.D	5.01 ± 1.13	5.82 ± 0.16	8.59 ± 1.83

$P < 0.0001$

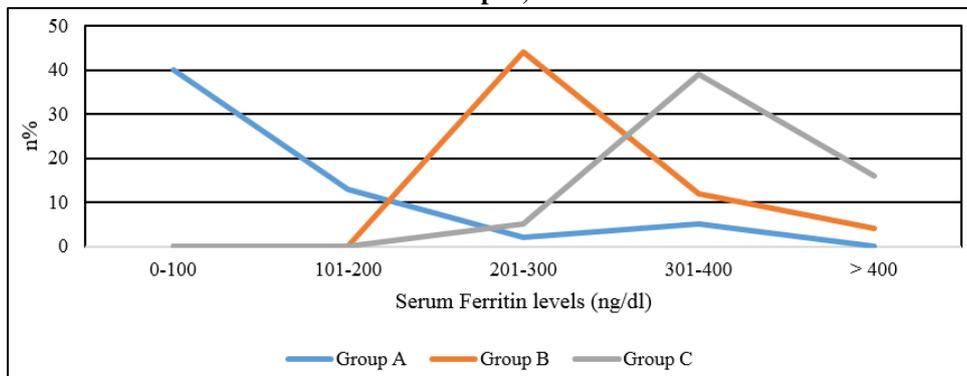**Graph 4: Distribution of serum ferritin levels in Group A, B & C**

Table 2: Correlation of serum ferritin levels in Group A, B & C

S. Ferritin (ng/dl)	Group A (n %)	Group B (n%)	Group C (n%)
0-100	40 (66)	0	0
101-200	13 (23)	0	0
201-300	2 (3)	44 (73)	5 (8)
301-400	5 (8)	12 (20)	39 (65)
>400	0	4 (7)	16 (27)
Mean ± S.D	112.08 ± 90.1	334.4 ± 39.1	368.9 ± 46.7
r value	0.48	0.361	0.55
p value	<0.001		

Graph 5: Scatter diagram - Correlation of HbA1c with serum ferritin levels in Group A, Group B and Group C
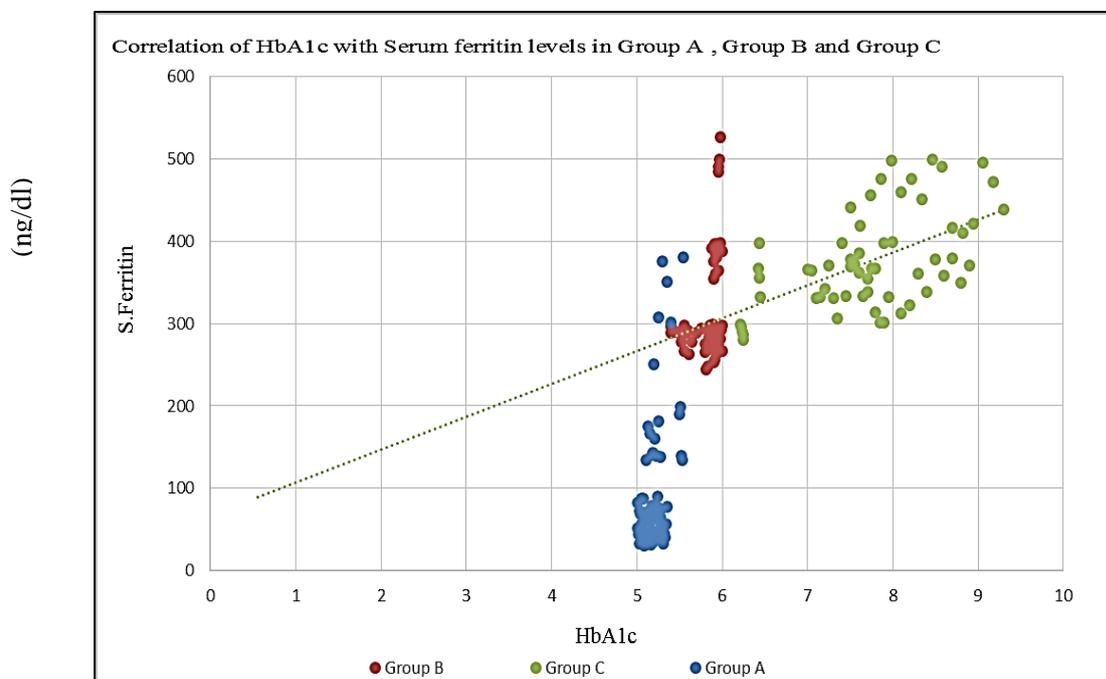
The serum ferritin levels are positively correlated with HbA1c levels and statistically significant.

Discussion

Type 2 diabetes mellitus is one of the largest metabolic disorders. Systemic inflammation is an predisposing factor for type 2 DM and atherosclerosis. Ferritin has been known as an index for body iron stores and also as an inflammatory marker.[2]

In the present study, in Group B & C had 50 females and 70 males in the diabetic group and in Group A, 37 were males and 23 were females.

We studied Glycated hemoglobin levels and serum ferritin in known type 2 diabetes subjects and healthy adults as controls.

In this study, 55% fell in the age group 41 to 50 years mean age being 42.5 years in the group A. Whereas 51.6% of subjects in the type 2 diabetic group were in the age group of 41-50 years with mean of 42.9 years age in diabetics with HbA1C <6mg/dl and 44.6 years in diabetics with HbA1C >6mg/dl.

In Group A, FBS levels were in the range of 87.74 ± 9.3 mg/dl. The mean ± SD of fasting serum glucose in Group B and Group C were 140.7 ± 17.3mg/dl and 167.85 ± 26.27 mg/dL, respectively. The mean value of fasting serum glucose was higher in Group B compared to Group C. The increase is found to be statistically highly significant (p <0.001) and is in accordance with previous studies.[5-7]

Marginal elevation of glucagon, increased synthesis and decreased utilization of glucose induces increased blood glucose levels in type 2 diabetes.[8] This leads to decreased utilization of glucose by the muscles and adipocytes and increased glucose synthesis by the liver and leading to hyperglycemia.

The mean ± SDs of HbA1c in controls was 5.01 ± 1.13mg/dl & type 2 diabetes were in the range of 5.82 ± 0.16 & 8.59 ± 1.83mg/dl in Group B & C respectively. The mean value of HbA1c was higher in type 2 diabetic subjects as compared to controls. The increase was statistically highly significant (p <0.001). This is in accordance with previous studies.[9-13] It was also observed that HbA1c level positively correlated with fasting serum glucose. This is in accordance with Meshram A et al,[14] Shetty J K et al[9] & Sultan S et al.[15]

We also found statistically significant positive correlation existed between HbA1c and ferritin levels. This is in lieu with current consideration of serum ferritin levels as the best index of metabolic control for diabetic patients in clinical setting.[16] It is also a predisposing factor in the risk of development of micro and macrovascular complications of type 2 DM.[17,18]

The most important factor governing the quantity of glycated hemoglobin formed is the prevailing plasma glucose concentration. As the plasma glucose concentration is increased in diabetic subjects, glycated hemoglobin also increased in diabetic subjects.

Glycated hemoglobin levels probably reflect the degree of glycemic control of the individual better than measuring fasting and post-prandial blood glucose levels. This is because glycated hemoglobin does not depend on variables such as patient co-operation, time of the day, stress, exercise, food intake or renal threshold. This makes attractive screening test in population studies.[19]

It represents the mean daily blood sugar concentration and degree of carbohydrate imbalance, better than fasting blood glucose concentrations or glucose tolerance test results. Hence it may provide a better index of control of diabetic patient without resorting to a glucose loading procedure.[20]

The mean ± SDs of ferritin in controls was 112.08 ± 90.1ng/dl and type 2 diabetic subjects were in the range of 334.4 ± 39.1ng/mL in diabetics with HbA1C < 6mg/dl and 368.9 ± 46.7 ng/ml in diabetics with HbA1C >6mg/dl respectively. The mean value of ferritin in type 2 diabetic subjects was higher when compared to controls. Serum ferritin positively correlates with HbA1c in group B & C with r values of 0.36 and 0.55 for Group B and Group C respectively. The increase was found to be statistically highly significant (p <0.001). This is in accordance with Sumeet Smotra et al.[4]

The mean value of ferritin in type 2 diabetic subjects was higher when compared to controls. The increase was found to be statistically highly significant (p <0.001). This is in accordance with the previous studies.[1, 21,22]

Excess iron deposition in the liver may cause IR by interfering with the ability of insulin to suppress hepatic glucose production. Iron is autoxidized to form highly reactive, lipid soluble iron-oxygen complexes. These free radicals are powerful pro-oxidants which can change membrane properties and result in tissue damage. In addition iron accumulation in hepatocytes may interfere with insulin extracting capacity of the liver, & affect insulin synthesis and secretion in pancreas. Iron excess probably contributes initially to IR and subsequently to decreased insulin secretion[21]

According to our results together with previous other studies findings, we suggest that the quantitative determination of serum ferritin help in predicting type 2 diabetes mellitus associated cardiovascular complications. Poorly controlled patients of DM have hyper ferritinemia which co-relates with diabetic retinopathy, diabetic nephropathy and vascular dysfunction.

Glycated hemoglobin provides a retrospective index of glucose control over a time in diabetic subjects. Measurement of glycated hemoglobin serves as a simple and rapid procedure to assess glycemic control. It serves both as a screening test for control of diabetes and as an indicator of efficacy of treatment. Thus the study concluded that inflammatory biomarker - ferritin is strongly and independently associated with cardiovascular complications in diabetes. In addition regular exercises and effective administration of anti-inflammatory agents may offer protection against type 2 diabetes mellitus associated complications.

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